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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/077,718	06/08/1998	HAKAN NYQVIST	1103326-0503	6402
22466	7590	11/19/2003	EXAMINER	
ASTRA ZENECA PHARMACEUTICALS LP GLOBAL INTELLECTUAL PROPERTY 1800 CONCORD PIKE WILMINGTON, DE 19850-5437			SOLOLA, TAOFIQ A	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/077,718	NYQVIST ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Taofiq A. Solola	1626	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 17 September 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 3-5, 12-18 and 20-54 is/are pending in the application.
- 4a) Of the above claim(s) 12-18, 20, 22, 25-33, 37-41, 45-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 3-5, 21, 23, 24, 34-36 and 42-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1</u> | 6) <input type="checkbox"/> Other: _____                                    |

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Claims 3-5, 12-18, 20-54 are pending in this application.

Claims 1-2, 6-11, 19 are canceled.

## DETAILED ACTION

### *Election/Restriction*

1. The Markush group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. For these reasons provided below, restriction to one of the following Groups is required under 35 U.S.C. 121, wherein a Group is a set of patentably distinct inventions of a broad statutory category (e.g. Compounds, Methods of Use, Methods of Making, etc.):

- I. Claims 3-5, 21, 23-24, 34-36, 42-44, drawn to tartrate salt and pharmaceutical compositions classified in several heterocyclic classes (514, 549) and numerous subclasses.
- II. Claims 12-15, 20, 25-30, 37-41, 45-49, drawn to various methods of use, classified in class 514, various subclasses.
- III. Claim 16-18, 22, 31-33, 50-53, drawn to a process of preparing tartrate salt, classified in several heterocyclic and non-heterocyclic classes and subclasses as defined in group I.
- IV. Claim 54, drawn to product-by-process of tartrate salt, classified in several heterocyclic and subclasses as defined in group I.

In accordance with the decisions in *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature

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disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 U.S.C. 103.

4. Where an election of any one of Groups I-IV is made, an election of a single compound (or set of compounds) is further required including an exact definition of each substitution on the base molecule (Formula #), wherein a single member at each substituent group or moiety is selected. For example, if a base molecule has a substituent group R1, wherein R1 is recited to be any one of H, OH, COOH, aryl, alkoxy, halogen, amino, etc., then applicant must select a single substituent of R1, for example OH or aryl, and each subsequent variable position. In the instant case, upon election of a single compound (or set of compounds), the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar thereto as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim which fall into the same class and subclass as the elected compound (or set of compounds), but may also include additional compounds which fall in related subclasses. Examination will then proceed on the elected compound AND the entire scope of the invention encompassing the elected compound as defined by common classification. A clear statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits. Note that the restriction requirement will not be made final until such time as applicant is informed of the full scope of compounds along with process of using said compound under examination. This will be set forth by reference to specific class(es) and subclass(es) examined. Should applicant traverse on the ground that the compounds are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C 103(a) of the other.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventors must be amended in compliance with 37C.F.R. 1.48(b) if one of the currently

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named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. 1.48(b) and by the fee required under 37CFR 1.17(i).

If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can **set forth** a group of compounds which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP 608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

***Rationale Establishing Patentable Distinctiveness Within Each Group***

Each Invention Set listed above is directed to or involves the use or making of

compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over either of the other inventions, i.e. they are patentable over each other. Chemical structures which are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holdings of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

***The above Groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:***

Groups III, IV and I are related as process of making and product made respectively.

The inventions are distinct if either or both of the following can be shown: (1) that the process as

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claimed can be used to make other and materially different product or (2) that the product can be made by another material different process (MPEP 806.05(f)). In the instant case, the product as claimed can be made by another materially process as demonstrated by Evenden et al., WO 95/11891

Groups I and II are related as product and method of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the method for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product (MPEP 806.05(h)). In the instant case, the product as claimed can be used in a materially different method of using that product as demonstrated throughout the specification and claims in group II which are directed to several different methods of using the product.

Each of the different methods of use inventions set forth in Group II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Methods of use are unrelated if one of three differences are found between them. These differences are 1) the population being treated, 2) the material being used, and 3) the methodology for treatment. If any one or more of these differences exist and are patentably distinct, then the methods are unrelated. In the instant case, the different methods of use are unrelated because the patient population treated for each method is divergent.

In addition, because of the plethora of classes and subclasses in each of the Groups, a serious burden is imposed on the examiner to perform a complete search of the defined areas.

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Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden in the examination of this application.

### ***Advisory of Rejoinder***

The following is a recitation of M.P.E.P. §821.04, Rejoinder:

Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02© and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either (1) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2), or (2) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2), even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26 states that "[m]oney paid by actual mistake or in excess will be refunded, but a mere change of purpose after the payment of money...will not entitle a party to demand such a return..." The fees paid under 37 CFR 1.129(b) were not paid by actual mistake nor paid in excess, therefore, applicant would not be entitled to a refund.

In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

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“However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined.” (emphasis added)

Therefore, in accordance with M.P.E.P. §821.04 and *In re Ochiai*, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone call to Kenneth Mitchell on 11/12/03 a provisional election was made without traversal to prosecute the invention of group I. Claims in groups II-IV, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).



***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 3-5, 21, 23-24, 34-36, 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 23, 34-36 are substantial duplicates of claim 3. Also, claims 21, 24, 42-44 are duplicates of claim 5. Claims 4, 23, 34-36, and 21, 24, 42-44 are written with physical and chemical properties of claim 3 (salt) and 5 (composition). According to the specification the salt of claims 3 and 5 have the recited properties in claims 4, 23, 34-36, and 21, 24, 42-44. Therefore, the dependent claims fail to further limit the scope of claims 3 and 5, while the independent claims are duplicates. Route of administration is not a limitation and therefore claim 21 is a duplicate of claim 5. By deleting claims 4, 23, 34-36, and 21, 24, 42-44 the rejection would be overcome.

The term "comprising" in claim 34 renders the claim indefinite. The term is open-ended. A compound claim must be referred to in close-ended terms such as consists or consisting.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 3-5, 21, 23-24, 34-36, 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evenden et al., WO 95/11891.

Applicants claim monohydrate of tartaric salt of (R)-3-N,N-dicyclobutylamino-8-fluoro-3,4-dihydro-2H-1-benzopyran-5-carboxamide, and their composition. In preferred embodiment the salt is characterized as stable, soluble and having "good dissolution properties," all well known properties of hydrate salts in general.

Determination of the scope and content of the prior art (MPEP §2141.01)

Evenden et al., teach similar compounds having general formula I (page 5, lines 1-20); their organic and inorganic acids salts, (page 6, line 37 to page 7, line 17) and their pharmaceutical preparations (compositions). See the abstract, page 11, lines 1-11. Evenden et al., teach tartaric acid salt as illustrative (example) of the salt. See page 7, lines 4-6, and that the salt can be "readily prepared by methods known in the art."

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant invention and that of Evenden et al., is that the tartaric salt is prepared in the instant as monohydrate while Evenden et al., do not prepare it. Also, the salt is characterized in the instant as stable, soluble and having "good dissolution properties" while Evenden et al., do not characterize it.

Finding of prima facie obviousness---rational and motivation (MPEP §2142.2413)

By preparing the hydrate of a well known salt and further characterizing such do not make the salt novel or patentable absent a novel and useful utility. The characterized properties are expected of hydrate salts in general. They are not unexpected. Also, applicant fails to submit a declaration that the salt would maintain its water of hydration in compositions. Otherwise, the composition not would be different from anhydrate salt.

Therefore, the instantly claimed invention is prima facie obvious from the teaching of Evenden et al. One of ordinary skill in the art would have known to make the monohydrate salt at the time this invention was made. The motivation to make the claimed salt is from the teaching of Evenden et al., that tartaric salt is an illustrative example, that it could be "readily prepared by methods known in the art," and from knowledge known in the art that hydrate salts are more stable than the anhydrate.

Applicant's arguments filed 9/17/03 have been fully considered but they are not persuasive. Applicant contends that the prior art of Evenden et al., fail to describe the instant salt as monohydrate. This is not persuasive for reason set forth above.

Applicant's amendment necessitated the restriction requirement presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

***Telephon Inquiry***

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Taofiq A. Solola whose telephone number is (703) 308-4690. The examiner is on flexible work schedule and is generally out of the office on Wednesdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (703) 308-4537. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

November 15, 2003

Group 1626  
for Robert W. Ransauer  
Taofiq A. Solola  
Primary Examiner  
Art Unit 1626